

Bile Duct Cancer



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General Information About Bile Duct Cancer (Cholangiocarcinoma)

KEY POINTS

- Bile duct cancer is a rare disease in which malignant (cancer) cells form in the bile ducts.
- Having colitis or certain liver diseases can increase the risk of bile duct cancer.
- Signs of bile duct cancer include jaundice and pain in the abdomen.
- Tests that examine the bile ducts and nearby organs are used to diagnose and stage bile duct cancer.
- Different procedures may be used to obtain a sample of tissue and diagnose bile duct cancer.
- Certain factors affect prognosis (chance of recovery) and treatment options.

Bile duct cancer is a rare disease in which malignant (cancer) cells form in the bile ducts.

A network of tubes, called ducts, connects the liver, gallbladder, and small intestine. This network begins in the liver where many small ducts collect bile (a fluid made by the liver to break down fats during digestion). The small ducts come together to form the right and left hepatic ducts which lead out of the liver. The two ducts join outside the liver and form the common hepatic duct. The cystic duct connects the gallbladder to the common hepatic duct. Bile from the liver passes through the hepatic ducts, common hepatic duct, and cystic duct and is stored in the gallbladder.

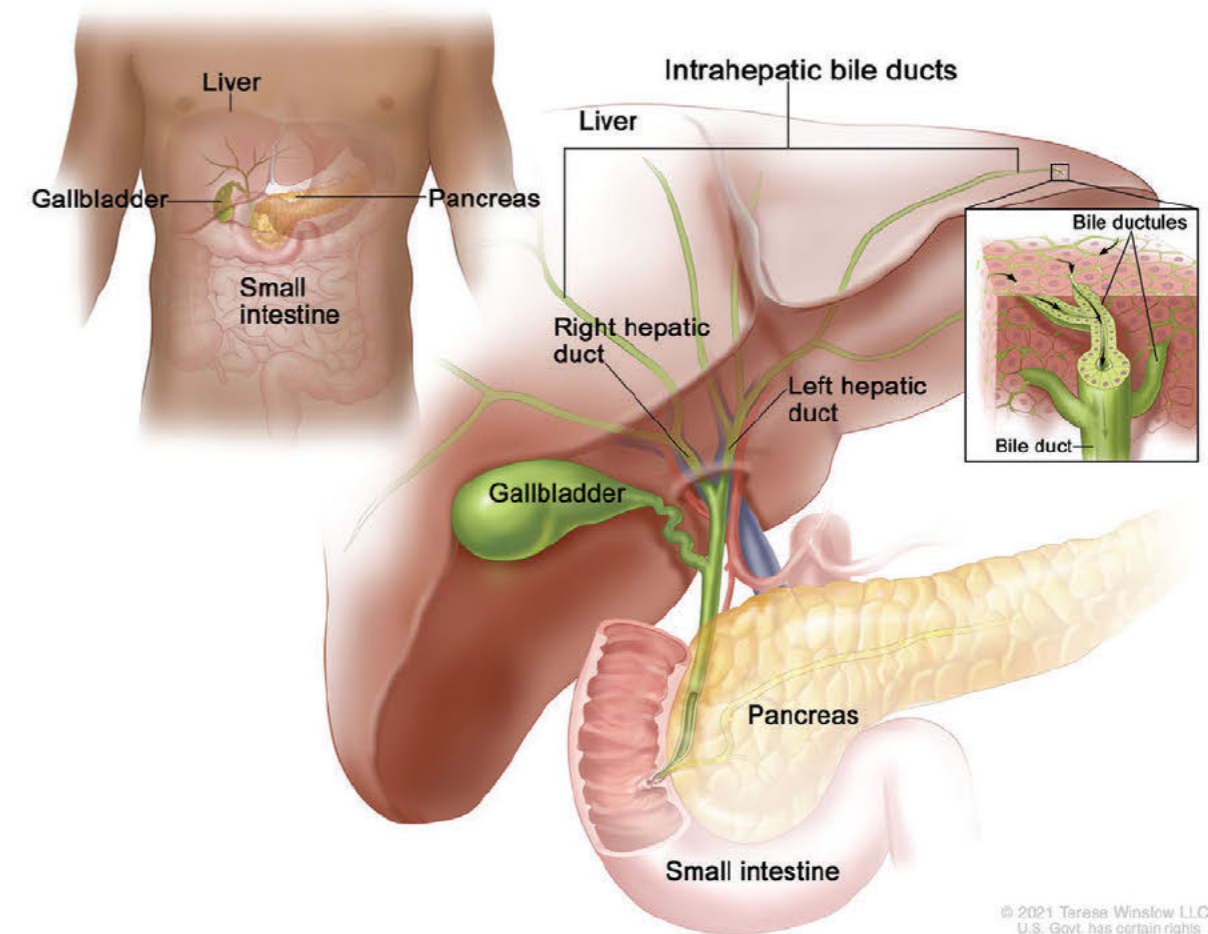
When food is being digested, bile stored in the gallbladder is released and passes through the cystic duct to the common bile duct and into the small intestine.

Bile duct cancer is also called **cholangiocarcinoma**.

Two Types of Bile Duct Cancer

- **Intrahepatic bile duct cancer:** This type of cancer forms in the bile ducts inside the liver. Only a small number of bile duct cancers are intrahepatic. Intrahepatic bile duct cancers are also called intrahepatic cholangiocarcinomas.

Anatomy of the Intrahepatic Bile Ducts

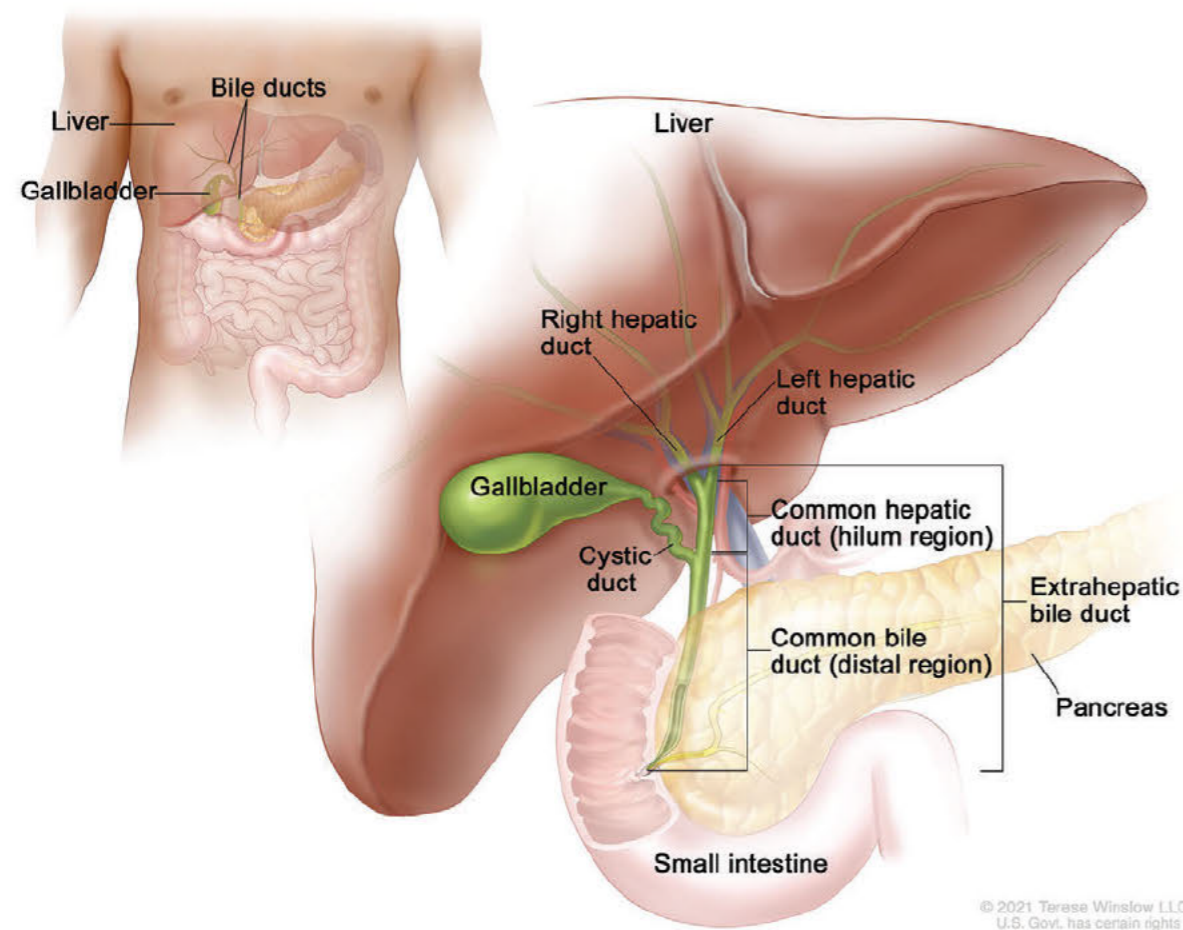


- **Extrahepatic bile duct cancer:** This type of cancer forms in the bile ducts outside the liver. The extrahepatic bile duct is made up of the hilum region and the distal region. Cancer can form in either region:

Perihilar bile duct cancer: This type of cancer is found in the hilum region, the area where the right and left bile ducts exit the liver and join to form the common hepatic duct. Perihilar bile duct cancer is also called a Klatskin tumor or perihilar cholangiocarcinoma.

Distal bile duct cancer: This type of cancer is found in the distal region. The distal region is made up of the common bile duct which passes through the pancreas and ends in the small intestine. Distal bile duct cancer is also called extrahepatic cholangiocarcinoma.

Anatomy of the Extrahepatic Bile Ducts



Having colitis or certain liver diseases can increase the risk of bile duct cancer.

Risk factors for bile duct cancer include the following conditions:

- Primary sclerosing cholangitis (a progressive disease in which the bile ducts become blocked by inflammation and scarring).
- Chronic ulcerative colitis.
- Cysts in the bile ducts (cysts block the flow of bile and can cause swollen bile ducts, inflammation, and infection).
- Infection with a Chinese liver fluke parasite.

Signs and Symptoms

These and other signs and symptoms may be caused by bile duct cancer or by other conditions. Check with your doctor if you have any of the following:

- Jaundice (yellowing of the skin or whites of the eyes).
- Dark urine.
- Clay colored stool.
- Pain in the abdomen.
- Fever.
- Itchy skin.
- Nausea and vomiting.
- Weight loss for an unknown reason.

Testing

Tests that examine the bile ducts and nearby organs are used to diagnose and stage bile duct cancer. The following are tests and procedures that may be used:

- **Physical exam and health history:** An exam of the body to check general signs of health including checking for signs of disease such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- **Liver function tests:** A procedure in which a blood sample is checked to measure the amounts of bilirubin and alkaline phosphatase released into the blood by the liver. A higher than normal amount of these substances can be a sign of liver disease that may be caused by bile duct cancer.
- **Laboratory tests:** Medical procedures that test samples of tissue, blood, urine, or other substances in the body. These tests help to diagnose disease, plan and check treatment, or monitor the disease over time.
- **Carcinoembryonic antigen (CEA) and CA 19-9 tumor marker tests:** A procedure in which a sample of blood, urine, or tissue is checked to measure the amounts of certain substances made by organs, tissues, or tumor cells in the body. Certain substances are linked to specific types of cancer when found in increased levels in the body. These are called tumor markers. Higher than normal levels of carcinoembryonic antigen (CEA) and CA 19-9 may mean there is bile duct cancer.
- **Ultrasound exam:** A procedure in which high energy sound waves (ultrasound) are bounced off internal tissues or organs such as the abdomen and make echoes. The echoes form a picture of body tissues called a sonogram. The picture can be printed to be looked at later.

- **CT scan (CAT scan):** A procedure that makes a series of detailed pictures of areas inside the body such as the abdomen that are taken from different angles. The pictures are made by a computer linked to an x ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- **MRI (magnetic resonance imaging):** A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- **MRCP (magnetic resonance cholangiopancreatography):** A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body such as the liver, bile ducts, gallbladder, pancreas, and pancreatic duct.

Cells and tissues may be removed during a biopsy so they can be viewed under a microscope by a pathologist to check for signs of cancer. The type of procedure used to obtain a biopsy depends on whether the patient is well enough to have surgery. Types of biopsy procedures include the following:

- **Laparoscopy:** A surgical procedure to look at the organs inside the abdomen such as the bile ducts and liver to check for signs of cancer. Small incisions (cuts) are made in the wall of the abdomen and a laparoscope (a thin, lighted tube) is inserted into one of the incisions. Other instruments may be inserted through the same or other incisions to perform procedures such as taking tissue samples to be checked for signs of cancer.
- **Percutaneous transhepatic cholangiography (PTC):** A procedure used to x ray the liver and bile ducts. A thin needle is inserted through the skin below the ribs and into the liver. Dye is injected into the liver or bile ducts, and an x ray is taken. A sample of tissue is removed and checked for signs of cancer. If the bile duct is blocked, a thin, flexible tube called a stent may be left in the liver to drain bile into the small intestine or a collection bag outside the body. This procedure may be used when a patient cannot have surgery.
- **Endoscopic retrograde cholangiopancreatography (ERCP):** A procedure used to x ray the ducts (tubes) that carry bile from the liver to the gallbladder and from the gallbladder to the small intestine. Sometimes bile duct cancer causes these ducts to narrow and block or slow the flow of bile which can cause jaundice. An endoscope is passed through the mouth and stomach and into the small intestine. Dye is injected through the endoscope (thin, tube like instrument with a light and a lens for viewing) into the bile ducts and an x ray is taken. A sample of tissue is removed and checked for signs of cancer. If the bile duct is blocked, a thin tube may be inserted into the duct to unblock it. This tube (or stent) may be left in place to keep the duct open. This procedure may be used when a patient cannot have surgery.
- **Endoscopic ultrasound (EUS):** A procedure in which an endoscope is inserted into the body usually through the mouth or rectum. An endoscope is a thin, tube like instrument with a light and a lens for viewing. A probe at the end of the endoscope is used to bounce high energy sound waves (ultrasound) off internal tissues or organs and make echoes. The echoes form a picture of body tissues called a sonogram. A sample of tissue is removed and checked for signs of cancer. This procedure is also called endosonography.

Prognosis Factors

Certain factors affect the prognosis (chance of recovery) and treatment options. The prognosis and treatment options depend on the following:

- Whether the cancer is in the upper or lower part of the bile duct system.
- The stage of the cancer (whether it affects only the bile ducts or has spread to the liver, lymph nodes, or other places in the body).
- Whether the cancer has spread to nearby nerves or veins.
- Whether the cancer can be completely removed by surgery.
- Whether the patient has other conditions such as primary sclerosing cholangitis.
- Whether the level of CA 19 9 is higher than normal.
- Whether the cancer has just been diagnosed or has recurred (come back).

Treatment options may also depend on the symptoms caused by the cancer. Bile duct cancer is usually found after it has spread and can rarely be completely removed by surgery. Palliative therapy may relieve symptoms and improve the patient's quality of life.

Stages of Bile Duct Cancer

KEY POINTS

- The results of diagnostic and staging tests are used to find out if cancer cells have spread.
- There are three ways that cancer spreads in the body.
- Cancer may spread from where it began to other parts of the body.
- Stages are used to describe the different types of bile duct cancer.
 - Intrahepatic bile duct cancer
 - Perihilar bile duct cancer
 - Distal bile duct cancer
- The following groups are used to plan treatment:
 - Resectable (localized) bile duct cancer
 - Unresectable (including metastatic and recurrent) bile duct cancer

Possible Spreading of Cancer

There are three ways that cancer spreads in the body. Cancer can spread through tissue, the lymph system, and the blood.

- **Tissue:** The cancer spreads from where it began by growing into nearby areas.
- **Lymph system:** The cancer spreads from where it began by getting into the lymph system. The cancer travels through the lymph vessels to other parts of the body.
- **Blood:** The cancer spreads from where it began by getting into the blood. The cancer travels through the blood vessels to other parts of the body.

Cancer may spread from where it began to other parts of the body. When cancer spreads to another part of the body, it is called metastasis. Cancer cells break away from where they began (the primary tumor) and travel through the lymph system or blood. The metastatic tumor is the same type of cancer as the primary tumor. For example, if bile duct cancer spreads to the liver, the cancer cells in the liver are actually bile duct cancer cells. The disease is metastatic bile duct cancer and not liver cancer.

Stages Used for Different Types of Bile Duct Cancer

Intrahepatic Bile Duct Cancer

Stage 0

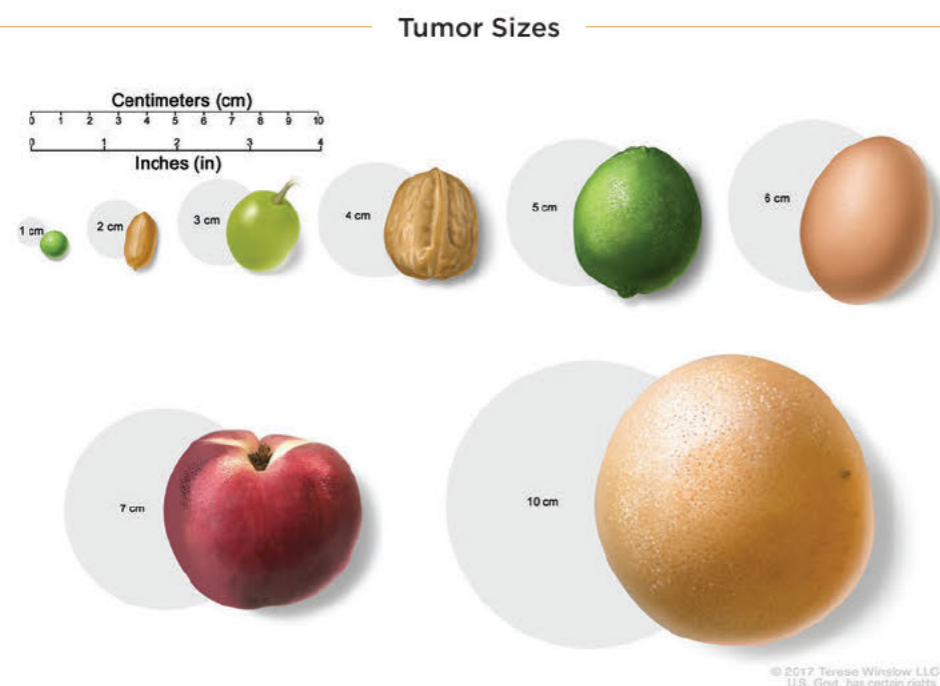
In stage 0 intrahepatic bile duct cancer, abnormal cells are found in the innermost layer of tissue lining the intrahepatic bile duct. These abnormal cells may become cancer and spread into nearby normal tissue. Stage 0 is also called carcinoma in situ.

Stage I

Stage I intrahepatic bile duct cancer is divided into stages IA and IB.

Stage IA: Cancer has formed in an intrahepatic bile duct, and the tumor is 5 centimeters or smaller.

Stage IB: Cancer has formed in an intrahepatic bile duct, and the tumor is larger than 5 centimeters.



Stage II

In stage II intrahepatic bile duct cancer, the tumor has either spread through the wall of an intrahepatic bile duct and into a blood vessel, or more than one tumor has formed in the intrahepatic bile duct and may have spread into a blood vessel.

Stage III

Stage III intrahepatic bile duct cancer is divided into stages IIIA and IIIB.

Stage IIIA: The tumor has spread through the capsule (outer lining) of the liver.

Stage IIIB: Cancer has spread to organs or tissues near the liver, such as the duodenum, colon, stomach, common bile duct, abdominal wall, diaphragm, or the part of the vena cava behind the liver, or the cancer has spread to nearby lymph nodes.

Stage IV

In stage IV intrahepatic bile duct cancer, cancer has spread to other parts of the body, such as the bone, lungs, distant lymph nodes, or tissue lining the wall of the abdomen and most organs in the abdomen.

Perihilar Bile Duct Cancer

Stage 0

In stage 0 perihilar bile duct cancer, abnormal cells are found in the innermost layer of tissue lining the perihilar bile duct. These abnormal cells may become cancer and spread into nearby normal tissue. Stage 0 is also called carcinoma in situ or high grade dysplasia.

Stage I

In stage I perihilar bile duct cancer, cancer has formed in the innermost layer of tissue lining the perihilar bile duct and has spread into the muscle layer or fibrous tissue layer of the perihilar bile duct wall.

Stage II

In stage II perihilar bile duct cancer, cancer has spread through the wall of the perihilar bile duct to nearby fatty tissue or to liver tissue.

Stage III

Stage III perihilar bile duct cancer is divided into stages IIIA, IIIB, and IIIC.

Stage IIIA: Cancer has spread to branches on one side of the hepatic artery or of the portal vein.

Stage IIIB: Cancer has spread to one or more of the following:

- The main part of the portal vein or its branches on both sides.
- The common hepatic artery.
- The right hepatic duct and the left branch of the hepatic artery or of the portal vein.
- The left hepatic duct and the right branch of the hepatic artery or of the portal vein.

Stage IIIC: Cancer has spread to 1 to 3 nearby lymph nodes.

Stage IV

Stage IV perihilar bile duct cancer is divided into stages IVA and IVB.

Stage IVA: Cancer has spread to 4 or more nearby lymph nodes.

Stage IVB: Cancer has spread to other parts of the body, such as the liver, lung, bone, brain, skin, distant lymph nodes, or tissue lining the wall of the abdomen and most organs in the abdomen.

Distal Bile Duct Cancer

Stage 0

In stage 0 distal bile duct cancer, abnormal cells are found in the innermost layer of tissue lining the distal bile duct. These abnormal cells may become cancer and spread into nearby normal tissue. Stage 0 is also called carcinoma in situ or high grade dysplasia.

Stage I

In stage I distal bile duct cancer, cancer has formed and spread fewer than 5 millimeters into the wall of the distal bile duct.

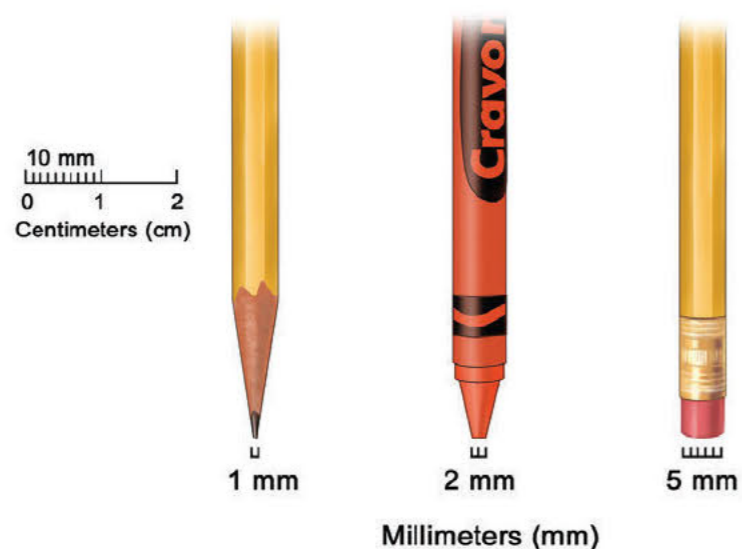
Stage II

Stage II distal bile duct cancer is divided into stages IIA and IIB.

Stage IIA: Cancer has either spread fewer than 5 millimeters into the wall of the distal bile duct and has spread to 1 to 3 nearby lymph nodes or 5 to 12 millimeters into the wall of the distal bile duct.

Stage IIB: Cancer has spread 5 millimeters or more into the wall of the distal bile duct. Cancer may have spread to 1 to 3 nearby lymph nodes.

Millimeter Examples



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Millimeters (mm). A sharp pencil point is about 1 mm, a new crayon point is about 2 mm, and a new pencil eraser is about 5 mm.

Stage III

Stage III distal bile duct cancer is divided into stages IIIA and IIIB.

Stage IIIA: Cancer has spread into the wall of the distal bile duct and to 4 or more nearby lymph nodes.

Stage IIIB: Cancer has spread to the large vessels that carry blood to the organs in the abdomen. Cancer may have spread to 1 or more nearby lymph nodes.

Stage IV

In stage IV distal bile duct cancer, cancer has spread to other parts of the body such as the liver, lungs, or tissue lining the wall of the abdomen and most organs in the abdomen.

The following groups are used to plan treatment:

- Resectable (localized) bile duct cancer
The cancer is in an area such as the lower part of the common bile duct or perihilar area where it can be removed completely by surgery.
- Unresectable (including metastatic and recurrent) bile duct cancer
Unresectable cancer cannot be removed completely by surgery. Most patients with bile duct cancer cannot have their cancer completely removed by surgery.

Metastasis is the spread of cancer from the primary site (place where it started) to other places in the body. Metastatic bile duct cancer may have spread to the liver, other parts of the abdominal cavity, or to distant parts of the body.

Recurrent bile duct cancer is cancer that has recurred (come back) after it has been treated. The cancer may come back in the bile ducts, liver, or gallbladder. Less often, it may come back in distant parts of the body.

Treatment Option Overview

KEY POINTS

- There are different types of treatments for patients with bile duct cancer.
- Three types of standard treatments are used:
 - Surgery
 - Radiation therapy
 - Chemotherapy
- New types of treatments are being tested in clinical trials:
 - Liver transplant
 - Targeted therapy
 - Immunotherapy
- Treatment for bile duct cancer may cause side effects.
- Patients may want to think about taking part in a clinical trial.
- Patients can enter clinical trials before, during, or after starting their cancer treatment.
- Follow up tests may be needed.

Treatment Options for Patients with Bile Duct Cancer

There are different types of treatments for patients with bile duct cancer. Some treatments are standard, and some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Patients may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment.

Three types of standard treatments are used:

Surgery

The following types of surgery are used to treat bile duct cancer:

- **Removal of the bile duct:** A surgical procedure to remove part of the bile duct if the tumor is small and in the bile duct only. Lymph nodes are removed, and tissue from the lymph nodes is viewed under a microscope to see if there is cancer.
- **Partial hepatectomy:** A surgical procedure in which the part of the liver where cancer is found is removed. The part removed may be a wedge of tissue, an entire lobe, or a larger part of the liver along with some normal tissue around it.
- **Whipple procedure:** A surgical procedure in which the head of the pancreas, the gallbladder, part of the stomach, part of the small intestine, and the bile duct are removed. Enough of the pancreas is left to make digestive juices and insulin.

After the doctor removes all of the cancer that can be seen at the time of the surgery, some patients may be given chemotherapy or radiation therapy after surgery to kill any cancer cells that are left. Treatment given after the surgery to lower the risk that the cancer will come back is called adjuvant therapy. It is not yet known whether chemotherapy or radiation therapy given after surgery helps keep the cancer from coming back.

The following types of palliative surgery may be done to relieve symptoms caused by a blocked bile duct and improve quality of life:

- **Biliary bypass:** If cancer is blocking the bile duct and bile is building up in the gallbladder, a biliary bypass may be done. During this operation, the doctor will cut the gallbladder or bile duct in the area before the blockage and sew it to the part of the bile duct that is past the blockage or to the small intestine to create a new pathway around the blocked area.
- **Endoscopic stent placement:** If the tumor is blocking the bile duct, surgery may be done to put in a stent (a thin tube) to drain bile that has built up in the area. The doctor may place the stent through a catheter that drains the bile into a bag on the outside of the body, or the stent may go around the blocked area and drain the bile into the small intestine.
- **Percutaneous transhepatic biliary drainage:** A procedure is used to x ray the liver and bile ducts. A thin needle is inserted through the skin below the ribs and into the liver. Dye is injected into the liver or bile ducts, and an x ray is taken. If the bile duct is blocked, a thin, flexible tube called a stent may be left in the liver to drain bile into the small intestine or a collection bag outside the body.

Radiation Therapy

Radiation therapy is a cancer treatment that uses high energy x rays or other types of radiation to kill cancer cells or keep them from growing. There are two types of radiation therapy:

- **External radiation therapy:** This type of radiation therapy uses a machine outside the body to send radiation toward the area of the body with cancer.
- **Internal radiation therapy:** This type of radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer.

It is not yet known whether external radiation therapy helps in the treatment of resectable bile duct cancer. In unresectable, metastatic, or recurrent bile duct cancer, new ways to improve the effect of external radiation therapy on cancer cells are being studied.

- **Hyperthermia therapy:** This type of therapy is a treatment in which body tissue is exposed to high temperatures to make cancer cells more sensitive to the effects of radiation therapy and certain anticancer drugs.
- **Radiosensitizers:** These are drugs that make cancer cells more sensitive to radiation therapy. Combining radiation therapy with radiosensitizers may kill more cancer cells.

Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells either by killing the cells or by stopping them from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the cerebrospinal fluid, an organ, or a body cavity such as the abdomen, the drugs mainly affect cancer cells in those areas (regional chemotherapy).

Systemic chemotherapy is used to treat unresectable, metastatic, or recurrent bile duct cancer. It is not yet known whether systemic chemotherapy helps in the treatment of resectable bile duct cancer.

In unresectable, metastatic, or recurrent bile duct cancer, intra arterial embolization is being studied. This is a procedure in which the blood supply to a tumor is blocked after anticancer drugs are given in blood vessels near the tumor. Sometimes, the anticancer drugs are attached to small beads that are injected into an artery that feeds the tumor. The beads block blood flow to the tumor as they release the drug. This allows a higher amount of drug to reach the tumor for a longer period of time which may kill more cancer cells.

Liver Transplant

In a liver transplant, the entire liver is removed and replaced with a healthy donated liver. A liver transplant may be done in patients with perihilar bile duct cancer. If the patient has to wait for a donated liver, other treatment is given as needed.

Targeted Therapy

Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells. Targeted therapies usually cause less harm to normal cells than chemotherapy or radiation therapy do.

Immunotherapy

Immunotherapy is a treatment that uses the patient's immune system to fight cancer. Substances made by the body or made in a laboratory are used to boost, direct, or restore the body's natural defenses against cancer. This cancer treatment is a type of biologic therapy.

- **Immune checkpoint inhibitor therapy:** This is a type of immunotherapy that may be used to treat bile duct cancer.

Clinical Trials

For some patients, taking part in a clinical trial may be the best treatment choice. Clinical trials are part of the cancer research process. Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment.

Many of today's standard treatments for cancer are based on earlier clinical trials. Patients who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment.

Patients who take part in clinical trials also help improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward.

Patients can enter clinical trials before, during, or after starting their cancer treatment.

Some clinical trials only include patients who have not yet received treatment. Other trials test treatments for patients whose cancer has not gotten better. There are also clinical trials that test new ways to stop cancer from recurring (coming back) or reduce the side effects of cancer treatment.

Follow-up tests may be needed.

Some of the tests that were done to diagnose the cancer or to find out the stage of the cancer may be repeated. Some tests will be repeated in order to see how well the treatment is working. Decisions about whether to continue, change, or stop treatment may be based on the results of these tests.

Some of the tests will continue to be done from time to time after treatment has ended. The results of these tests can show if your condition has changed or if the cancer has recurred (come back). These tests are sometimes called follow up tests or check ups.

Treatment of Resectable (Localized) Bile Duct Cancer

Treatment of resectable intrahepatic bile duct cancer may include:

- Surgery to remove the cancer which may include partial hepatectomy.
- Embolization may be done before surgery.

Treatment of resectable perihilar bile duct cancer may include:

- Surgery to remove the cancer which may include partial hepatectomy.
- Stent placement or percutaneous transhepatic biliary drainage as palliative therapy to relieve jaundice and other symptoms and improve the quality of life.

Treatment of resectable distal bile duct cancer may include:

- Surgery to remove the cancer which may include a Whipple procedure.
- Stent placement or percutaneous transhepatic biliary drainage as palliative therapy to relieve jaundice and other symptoms and improve the quality of life.

Adjuvant therapy for resectable bile duct cancer may include:

- Chemotherapy
- External beam radiation therapy
- A clinical trial of adjuvant therapy

Treatment of Unresectable Bile Duct Cancer (Including Metastatic or Recurrent Disease)

Treatment of unresectable bile duct cancer (including metastatic or recurrent disease) may include:

- Stent placement or biliary bypass as palliative treatment to relieve symptoms and improve the quality of life.
- External or internal radiation therapy as palliative treatment to relieve symptoms and improve the quality of life.
- Combination chemotherapy.
- A clinical trial of various combinations of chemotherapy.
- A clinical trial of immunotherapy in patients with mutations (changes) in certain genes.
- A clinical trial of targeted therapy for patients with mutations (changes) in certain genes.

Check the list of NCI supported cancer clinical trials that are now accepting patients with the bile duct cancer stage you are experiencing. For more specific results, refine the search by using other search features such as the location of the trial, the type of treatment, or the name of the drug. Talk with your doctor about clinical trials that may be right for you. General information about clinical trials is available from the following NCI website:

www.cancer.gov/about_cancer/treatment/clinical_trials

Notes

For more information and related links visit: www.cancer.gov/types/liver

Resource: PDQ® Adult Treatment Editorial board. PDQ Bile Duct Cancer Treatment. Bethesda, MD: National Cancer Institute. Available at <https://www.cancer.gov/types/liver/patient/bile-duct-treatment-pdq>. Accessed 08/06/2021.

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